

REMARKS

INTRODUCTORY COMMENTS:

In the Office Action under reply, the Examiner rejected all claims as follows:

(1) Claims 79-87 and 152-154 are rejected under 35 U.S.C. §112, second paragraph, as indefinite;

(2) Claim 1-3, 5, 6, 9-11, 16-25, 29-34, 36, 37, 39, 40, 46-66, 69, 72-86, 145, and 151-155 are rejected 35 U.S.C. §102(e) as anticipated by U.S. Patent Application Publication No. 2002/0094582 to Williams et al.;

(3) Claims 4, 7, 8, 12-15, 26-28, 38, 41-44, 67, 68, 70, 71, 87-106, 112-125, 135-144, and 146-148 are rejected under 35 U.S.C. §103(a) as obvious over Williams et al.

(4) Claims 107-111 are rejected under 35 U.S.C. §103(a) as obvious over Williams et al. in view of U.S. Patent No. 5,306,412 to Whitehouse et al.;

(5) Claims 126-133 are rejected 35 U.S.C. §101 for statutory-type double patenting over claim 105-112 of U.S. Patent Application Serial No. 09/784,705, now issued as U.S. Patent No. 6,603,118 to Ellson et al.

(6) Claim 134 is rejected under the judicially created doctrine of obviousness-type double patenting over claim 29 of U.S. Patent Application Serial No. 09/784,705, now U.S. Patent No. 6,603,118 to Ellson et al.;

(7) Claims 151-153 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 33-35 of U.S. Patent Application Serial No. 10/087,372 in view of claim 20 of the same application; and

(8) Claims 160 and 161 are rejected under 35 U.S.C. §103(a) as obvious over U.S. Patent No. 6,503,454 to Hadimioglu et al. in view of U.S. Patent No. 5,877,580 to Swierkowski.

The rejections are addressed in part by the above amendments to the claims and are otherwise traversed for reasons that will be discussed in detail below.

THE ABOVE AMENDMENTS:

In order to expedite prosecution, claims 39, 40, 43, 51-53, 66-68, 75, 77-125, 135-144, 160, and 161 have been canceled. Cancellation of these claims is without prejudice, without intent to limit the scope of the invention as claimed, and without acquiescing in the Examiner's rejection.

Independent claim 1 has been amended to correspond to independent claim 126. Independent claim 126 is directed to a method for preparing a sample molecule for analysis and is similar, but not identical, to claim 1 of Ellson et al., from which the subject application claims priority. Upon review of these claims, it should be apparent that device claim 1 parallels method claim 126 and that the device of claim 1 may be employed to carry out the method of claim 126.

Independent claim 145 has been amended to clarify that the inventive method may involve the preparation of a *contiguous* sample surface for analysis. Correspondingly, independent device claim 57 has been similarly amended so as to set forth a device for preparing a contiguous samples surface for analysis. These amendments are supported, for example, on page 43, line 20, to page 44, line 4.

A number of claims have been amended to depend directly or indirectly from the above-discussed independent claims, to correct obvious typographical errors, and to provide proper antecedent basis for all claim elements.

Support for the new dependent claims can be found, for example, on page 44, lines 19-25.

Thus, no new matter has been introduced by way of any these amendments and entry thereof is proper.

Upon entry of these amendments, claims are pending. For the Examiner's convenience, the pending claims upon entry of these amendments are listed in a suggested order for issuance in Appendix A.

STATUS OF THE CLAIMS

Claims 1-38, 41, 42, 44-50, 54-65, 69-74, 76, 126-134, 145-159, and 162-179 are pending. Claims 39, 40, 43, 51-53, 66-68, 75, 78-125, 135-144, 160, and 161 are canceled. Claims 1, 2, 5-8, 12, 15, 21-24, 32, 36, 44-46, 50, 57-64, 65, 76, 126-134, 145, 152-154, 156, and 157 are amended. Claims 162-179 are newly added. Claims 3, 4, 9-11, 13, 14, 16-20, 25-31, 33-35, 37, 42, 47-49, 54-56, 62, 63, 69-74, 146-151, 155, 158, and 159 are unchanged.

THE 35 U.S.C. §112, SECOND PARAGRAPH, INDEFINITENESS REJECTION:

Claims 79-87 and 152-154 are rejected under 35 U.S.C. §112, second paragraph, as indefinite. In issuing this rejection, the Examiner objected to the term "optionally." In addition, the Examiner noted a number of terms lacked proper antecedent basis. With the above-

amendments, the claims containing the objected-to terminology have been canceled and proper antecedent basis corrections have been made. Accordingly, withdrawal of this rejection is requested.

THE REJECTIONS OVER WILLIAMS ET AL. OPTIONALLY IN VIEW OF WHITEHOUSE ET AL.:

Claims 1-3, 5, 6, 9-11, 16-25, 29-34, 36, 37, 39, 40, 46-66, 69, 72-86, 145, and 151-155 are rejected 35 U.S.C. §102(e) as anticipated by U.S. Patent Application Publication No. 2002/0094582 to Williams et al. Similarly, claims 4, 7, 8, 12-15, 26-28, 38, 41-44, 67, 68, 70, 71, 87-106, 112-125, 135-144, and 146-148 are rejected under 35 U.S.C. §103(a) as obvious over Williams et al. In support of this rejection, the Examiner cites the same sections of Williams et al. and Whitehouse et al. and raises substantially the same issues in the Office Action of December 12, 2002, for the parent application, now U.S. Patent 6,603,118 to Ellson et al.

In response, applicants point out that a number of these claims have been canceled or rewritten so as to render the Examiner's rejection moot. To the extent that the rejection is applicable to the pending claims, applicants traverse the rejection for the reasons pointed out during the prosecution of Ellson et al.

Turning to the independent method claim 126 and claims depending therefrom, applicants respectfully traverse the rejection on the ground that Williams et al. neither discloses nor suggests all elements of claim 126, and Whitehouse et al. does not cure the deficiencies of Williams et al. As discussed above, claim 126 is similar, but not identical to claim 1 of Ellson et al. The claim is directed to a method that requires two distinct events to occur in succession. First, focused acoustic energy must be applied so that a droplet is ejected from a reservoir and an analyte molecule is deposited on a substrate surface. Then, sufficient energy is applied to ionize and release the analyte molecule from the substrate surface. Although Williams et al. describes the use of focused acoustic energy in the context of mass spectrometry, Williams et al. does not disclose a method that requires the two events to occur in succession.

In addition, paragraphs [0028] and [0029] of Williams et al. generally describe "source fluids" and "source fluid container structures." Williams et al. states that acoustic radiation may be used to eject droplets from fluids and containers and briefly mentions, in passing, the possible use of the disclosed method to form an array in paragraph [0071]. Williams et al. also mentions the possibility of ionizing droplets upon ejection from fluid containers, which would occur

during array preparation. However, there is no disclosure relating to the preparation of an array of analyte molecules on a surface using focused acoustic radiation *followed* by the successive application of sufficient energy to each site of the array to ionize the analyte molecules and release the analyte molecules from the substrate surface for analysis.

Thus, the disclosure contained in Williams et al. does not render the claims obvious. Applicants further point out that the disclosure in Williams et al. regarding the use of acoustic radiation, is generally limited to the ejection of droplets from *a source directly to a target*. For example, Williams et al. sets forth that ionized droplets may be ejected from a plurality of source fluids in an array directly into a mass spectrometer. That is, *Williams et al. merely describes a single-step method* for ejecting droplets of fluid from a source toward a target. In contrast, claim 126 and claims depending therefrom are directed to a method that involves two distinct steps: (a) using focused acoustic energy to deposit a sample molecule at a designated site on a substrate surface; and (b) applying energy to the designated site to ionize and release the molecule from the substrate surface.

Similarly, independent device claim 1 of the subject application and claims depending therefrom, parallel the method claim 126 and the claims depending therefrom.

Thus, it should be apparent that method claim 126 of the subject application generally parallels claim 1 of Ellson et al., and that device claim 1 of the subject application generally parallels claim 29 of Ellson et al. Since the pending claims set forth novel and nonobvious elements that are similar to those of the issued claims of Ellson et al., claims 1 and 126, the claims depending therefrom should be novel and nonobvious as well.

Turning to the independent method claim 145 and claims depending therefrom, applicants respectfully traverse the rejection as well. A number of elements serve to distinguish the subject matter of the claims from the disclosures of Williams et al. and Whitehouse et al. For example, claim 145 and all claims depending therefrom involve the ejection of a droplet of fluid toward a (1) *designated site on* (2) *a contiguous surface of a sample*. Applicants submit that neither of these enumerated elements are disclosed in or suggested by Williams et al. As discussed in the specification on page 22, lines 15-25, these elements are useful for performing analytical functions such as surface imaging and characterization of site-specific surface properties on a contiguous surface. Williams et al. neither discloses nor suggests these analytical functions.

The Examiner has erred by failing to consider the "*designated site*" element set forth in the claims. This element indicates that subject matter of the pending claims does not, as the Examiner appears to indicate, merely involve employing focused acoustic energy to establish contact between a cell surface and a selected molecule. Instead, the ejected droplet must be deposited on at least one *designated site*. Applicants submit that the *location specificity* set forth in the pending claims for the placement of an ejected droplet is neither disclosed nor suggested in Williams et al.

In addition, the pending claims set forth that the sample surface for receiving the ejected droplet is *contiguous*. In contrast, Williams et al. does not disclose a contiguous sample surface. Instead, as indicated in the Abstract, Williams et al. generally describes the transfer of fluids from an array of source sites to an array of target sites. As indicated in paragraph [0004], the target, like a multiwell plate fluid source, "may comprise thousands of loci that need to be accessed in a rapid, contamination-free manner." By emphasizing the deposition of different fluids at different locations, e.g., wells of well plates, and the need to prevent contamination, e.g., preventing the fluids from mixing between wells, Williams et al. teaches a method that uses a plurality of *discrete* target surfaces. That is, Williams et al. teaches away from the use of any contiguous sample surface.

In sum, although Williams et al. mentions that droplets can be deposited in an array of discrete targets to establish contact between the droplets and the targets, Williams et al. fails to disclose or suggest subject matter involving the ejection of a droplet of fluid toward a *designated site on a contiguous surface of a sample* so as to effect site-specific analysis on the contiguous surface. Upon review of claim 57 as amended, it should be apparent that this claim corresponds to independent method claim 145, as they both involve the preparation of a contiguous sample surface through the deposition of droplets on designated sites thereon. Thus, Williams et al. also fails to anticipate or render obvious independent device claim 57 and claims depending therefrom. Thus, withdrawal of all rejections over Williams et al. is warranted and requested.

THE DOUBLE PATENTING REJECTION OVER ELLSON ET AL.:

Claims 126-133 are rejected 35 U.S.C. §101 for statutory-type double patenting over certain claims of Ellson et al., and claim 134 is rejected under the judicially created doctrine of obviousness-type double patenting over another claim the same patent. In issuing the statutory-

type double patenting rejection, the Examiner states that claims 126-133 are identical in scope to certain method claims of Ellson et al. In addition, while admitting that pending claim 134 is not identical to any claims of Ellson et al., the Examiner nevertheless states that claim 134 is not patentably distinct from the claims of Ellson et al.

In response, applicants have rewritten claims 126-133 so that the claims differ in scope from the claims of Ellson et al. In addition, applicants are willing to disclaim the term of any patent issuing from this application that extends beyond the term of Ellson et al., in order to expedite prosecution. Accordingly, applicants submit herewith a signed terminal disclaimer to overcome the obviousness-type double patenting rejection. Thus, the double-patenting rejections over Ellson et al. should be withdrawn.

THE PROVISIONAL DOUBLE PATENTING REJECTION OVER U.S.S.N. 10/087,372:

Claims 151-153 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting over claims 33-35 of U.S. Patent Application Serial No. 10/087,372 in view of claim 20 of the same application. Again not wishing to acquiesce in the Examiner's provisional rejection, applicants are willing to disclaim the term of any patent issuing from this application that extends beyond the term of any patent issuing from U.S. Patent Application Serial No. 10/087,372, in order to expedite prosecution,. Accordingly, applicants are willing to submit a signed terminal disclaimer to overcome the obviousness-type double patenting rejection when notified that the pending claims are otherwise allowable. A copy of an unsigned terminal disclaimer is submitted herewith for the Examiner's review.

THE OBVIOUSNESS REJECTION OVER HADIMIOGLU ET AL. IN VIEW OF SWIERKOWSKI

Claims 160 and 161 are rejected under 35 U.S.C. §103(a) as obvious over U.S. Patent No. 6,503,454 to Hadimioglu et al. in view of U.S. Patent No. 5,877,580 to Swierkowski. As all other pending claims should be in shape for allowance, applicants have canceled these claims to expedite prosecution and preserved the right to file a continuation application directed to canceled subject matter without prejudice.

CONCLUSION

For all of the above reasons, it is submitted that the pending claims define an invention that is patentable over the art. As the application should now be in condition for allowance, a prompt indication to that effect would be appreciated.

If the Examiner has any questions concerning this communication, he is welcome to contact the undersigned attorney at (650) 330-0900.

Respectfully submitted,

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APPENDIX A

PENDING CLAIMS UPON ENTRY OF AMENDMENT

(LISTED IN ORDER OF PROPOSED CLAIM DEPENDENCIES)

1. (currently amended) ~~In a A device having a sample vessel for processing and/or analyzing preparing a sample molecule for processing and/or analysis,~~ the improvement comprising employing:

a reservoir holding a fluid ~~sample~~ comprised of the sample molecule;

an ejector comprising an acoustic radiation generator for generating acoustic radiation and a focusing means for focusing the acoustic radiation at a focal point near the surface of the fluid ~~sample~~; and

a means for positioning the ejector in acoustic coupling relationship to the reservoir to eject a droplet of the fluid ~~therefrom; sample into the sample vessel.~~

a substrate having a designated site on a surface thereof adapted to receive a droplet of fluid from the reservoir;

a means for positioning the substrate relative to the reservoir so that the designated site on the substrate surface is placed in droplet-receiving relationship to the reservoir, thereby allowing deposition of the analyte molecule thereon; and

a means for applying energy to the designated site in a manner sufficient to ionize the analyte molecule and to release the analyte molecule from the substrate surface for analysis.

2. (currently amended) The device of claim 1, ~~wherein the sample vessel is further comprising an ionization chamber in position to receive the ionized and released analyte molecule.~~

3. (original) The device of claim 2, wherein the device is a mass spectrometer.

4. (original) The device of claim 3, wherein the mass spectrometer is a time-of-flight mass spectrometer.

5. (currently amended) The device of claim 1, wherein the fluid ~~sample~~ occupies a volume of no more than about 100 μ L.

6. (currently amended) The device of claim 5, wherein the fluid ~~sample~~ occupies a volume of no more than about 10 μ L.

7. (currently amended) The device of claim 6, wherein the fluid ~~sample~~ occupies a volume of no more than about 1 μ L.

8. (currently amended) The device of claim 7, wherein the fluid ~~sample~~ occupies a volume of about 10 pL to about 100 nL.

9. (original) The device of claim 1, wherein the ejector is configured to eject a droplet having a volume of no more than about 1 nL.

10. (original) The device of claim 9, wherein the ejector is configured to eject a droplet having a volume of no more than about 1 pL.

11. (original) The device of claim 10, wherein the ejector is configured to eject a droplet having a volume of no more than about 100 fL.

12. (currently amended) The device of claim 1, wherein the ejector is configured to eject no more than about 5 percent of the fluid ~~sample~~ in the reservoir per droplet.

13. (original) The device of claim 1, wherein the sample molecule has a molecular weight of about 100 daltons to about 100 kilodaltons.

14. (original) The device of claim 13, wherein the molecular weight is about 1 to about 100 kilodaltons.

15. (currently amended) The device of claim 1, wherein the fluid ~~sample~~ further comprises water.

16. (original) The device of claim 1, wherein the sample molecule is nonmetallic.

17. (original) The device of claim 16, wherein the sample molecule is an organic compound.

18. (original) The device of claim 17, wherein the organic compound is a biomolecule.

19. (original) The device of claim 18, wherein the biomolecule is nucleotidic

20. (original) The device of claim 18, wherein the biomolecule is peptidic.

21. (currently amended) The device of claim 1, further comprising a detector for detecting reflected acoustic radiation from the fluid ~~sample~~.

22. (currently amended) The device of claim 2, further comprising a charging means for electrically charging the fluid ~~sample~~.

23. (currently amended) The device of claim 22, wherein the charging means is configured to electrically charge the surface of the fluid ~~sample~~.

24. (currently amended) The device of claim 22, wherein the charging means is configured to electrically charge the entire fluid ~~sample~~.

25. (original) The device of claim 22, further comprising a charged surface within the ionization chamber that attracts or repels the droplet.

26. (original) The device of claim 25, wherein the charged surface is a surface of a multipole analyzer.

27. (original) The device of claim 26, wherein the multipole analyzer is a quadrupole analyzer.

28. (original) The device of claim 2, wherein the reservoir is located within the ionization chamber.

29. (original) The device of claim 1, wherein the sample vessel comprises a microfluidic device.

30. (original) The device of claim 1, wherein the sample vessel represents a portion of a microfluidic device.

31. (original) The device of claim 30, wherein the reservoir represents a portion of an additional microfluidic device.

170. (new) The device of claim 1, wherein the means for applying energy comprises a source of photons, electrons, ions, or combinations thereof.

171. (new) the device of claim 170, wherein the means for applying energy comprises a source of photons.

172 (new) The device of claim 171, wherein the means for applying energy comprises a laser.

173. (new) The device of claim 170, wherein the means for applying energy comprises a source of electrons.

174. (new) The device of claim 170, wherein the means for applying energy comprises a source of ions.

57. (currently amended) ~~In a device having a sample vessel for processing and/or analyzing a plurality of sample molecules, the improvement comprising employing for preparing a contiguous sample surface for analysis:~~

a plurality of reservoirs each reservoir holding an analysis-enhancing fluid sample comprised of a sample molecule;

an ejector comprising an acoustic radiation generator for generating acoustic radiation and a focusing means for focusing the acoustic radiation at a focal point near the surface of the analysis-enhancing fluid sample; and

a means for positioning the ejector in acoustic coupling relationship to each of the reservoirs the reservoir to eject a droplet of the analysis-enhancing fluid therefrom sample into the sample vessel

a sample having a designated site on a contiguous surface thereof adapted to receive a droplet of the analysis-enhancing fluid from the reservoir, wherein the designated site contains an analyte molecule;

a means for positioning the sample so that the designated site on the contiguous sample surface is placed in droplet-receiving relationship to the reservoir, thereby allowing deposition of the analysis-enhancing fluid thereon; and

a means for applying energy to the designated site in a manner sufficient to ionize the analyte molecule and to release the analyte molecule from the designated site for analysis.

58. (currently amended) The device of claim 57, ~~wherein the sample vessel is further comprising~~ an ionization chamber in position to receive the ionized and released analyte molecule.

59. (currently amended) The device of claim ~~57~~58, wherein the device is a mass spectrometer.

60. (currently amended) The device of claim 57, ~~wherein the~~ comprising a plurality of reservoirs are arranged in an array.

61. (currently amended) The device of claim 57, ~~wherein the~~ comprising a plurality of reservoirs ~~are~~ provided as integrated members of a single substrate.

62. (original) The device of claim 61, wherein the reservoirs comprise designated sites on a surface of the substrate surface.

63. (original) The device of claim 62, wherein the substrate surface is substantially flat.

64. (currently amended) The device of claim 57, wherein ~~at least one~~ the sample molecule is a biomolecule.

65. (currently amended) The device of claim 57, further comprising a detector for detecting reflected acoustic radiation from the fluid ~~sample in the reservoir.~~ sample in the reservoir.

69. (original) The device of claim 58, further comprising a charged surface within the ionization chamber.

70. (original) The device of claim 69, wherein the charged surface is a surface of a multipole analyzer.

71. (original) The device of claim 70, wherein the multipole analyzer is a quadrupole analyzer.

72. (original) The device of claim 57, wherein the device comprises 96 reservoirs.

73. (original) The device of claim 72, wherein the device comprises 384 reservoirs.

74. (original) The device of claim 73, wherein the device comprises 1536 reservoirs.

76. (currently amended) The device of claim 57, ~~wherein the sample vessel comprises~~
further comprising a microfluidic device in position to receive the ionized and released analyte
molecule.

175. (new) The device of claim 57, wherein the means for applying energy comprises a
source of photons, electrons, ions, or combinations thereof.

176. (new) the device of claim 175, wherein the means for applying energy comprises a
source of photons.

177. (new) The device of claim 176, wherein the means for applying energy comprises a
laser.

178. (new) The device of claim 175, wherein the means for applying energy comprises a
source of electrons.

179. (new) The device of claim 175, wherein the means for applying energy comprises a
source of ions.

126. (currently amended) A method for preparing a ~~plurality of sample molecules~~ sample
molecule for analysis, comprising:

(a) ~~preparing an array comprised of a plurality of sample molecules on a substrate surface~~
~~by applying focused acoustic energy to each of a plurality of fluid-holding reservoirs, each of~~
~~said reservoirs holding~~ reservoir to eject a droplet of fluid containing a sample molecule in a
fluid to be applied therefrom to a designated site on ~~the~~ substrate surface; and

(b) ~~successively~~ applying sufficient energy to each ~~the~~ site to ionize ~~the sample molecules~~
and release the sample ~~molecules~~ molecule from the substrate surface for analysis.

127. (currently amended) The method of claim ~~126~~ 162, wherein step (b) comprises
bombarding ~~at least one~~ the site with photons.

128. (currently amended) The method of claim 127, wherein photonic bombardment is carried out using a laser.

129. (currently amended) The method of claim 126, wherein step (b) comprises bombarding ~~at least one~~ the site with electrons.

130. (currently amended) The method of claim 126, wherein step (b) comprises bombarding ~~at least one~~ the site with ions.

131. (currently amended) The method of claim 126, wherein step (b) comprises heating at ~~least one~~ the site.

132. (currently amended) The method of claim 126, wherein step (b) comprises directing focused acoustic energy to ~~at least one~~ the site.

133. (currently amended) The method of claim 126, wherein step (b) comprises passing an electrical current through ~~at least one~~ the site.

134. (currently amended) The method of claim 126, further comprising, after step (b), determining the mass of the ionized sample ~~molecules~~ molecule.

32. (currently amended) ~~A~~ The method of claim 126, wherein the for introducing a sample molecule is introduced into a sample vessel of a device for processing and/or analyzing a ~~the~~ sample molecule, comprising:

- ~~(a) providing a reservoir holding a fluid sample comprised of the sample molecule; and~~
- ~~(b) directing focused acoustic radiation at a point near the surface of the fluid sample to eject a droplet of the fluid sample from the surface of the fluid sample along a predetermined trajectory into the sample vessel of the device.~~

33. (original) The method of claim 32, wherein the sample vessel is an ionization chamber.

34. (original) The method of claim 33, wherein the device is a mass spectrometer.

35. (original) The method of claim 34, wherein the mass spectrometer is a time-of-flight mass spectrometer.

36. (currently amended) The method of claim ~~32~~126, further comprising repeating step ~~(b)~~(a).

37. (original) The method of claim 36, wherein the ejected droplets are substantially identical in size.

38. (currently amended) The method of claim 36, wherein no more than about 5 percent of the ~~sample~~ fluid in the reservoir is ejected per droplet.

41. (currently amended) The method of claim ~~32~~126, wherein the sample molecule has a molecular weight of about 100 daltons to about 100 kilodaltons.

42. (original) The method of claim 41, wherein the molecular weight is about 1 to about 100 kilodaltons.

44. (currently amended) The method of claim ~~32~~126, wherein the fluid ~~sample~~ further comprises water.

45. (currently amended) The method of claim ~~32~~126, wherein the sample molecule is nonmetallic.

46. (currently amended) The method of claim ~~45~~126, wherein the sample molecule an organic compound.

47. (original) The method of claim 46, wherein the organic compound is a biomolecule.

48. (original) The method of claim 47, wherein the biomolecule is nucleotidic.

49. (original) The method of claim 47, wherein the biomolecule is peptidic.

50. (currently amended) The method of claim ~~32~~126, further comprising, ~~after step (a)~~
~~and before step (b)~~(a), (a') transmitting acoustic radiation through the fluid ~~sample~~in the reservoir
and detecting for reflected acoustic radiation.

54. (original) The method of claim 32, wherein the sample vessel comprises a
microfluidic device.

55. (original) The method of claim 32, wherein the sample vessel represents a portion of
a microfluidic device.

56. (original) The method of claim 55, wherein the reservoir represents a portion of an
additional microfluidic device.

162. (new) The method of claim 126, wherein step (b) comprises bombarding at least one
site with photons, electrons, ions, or combinations thereof.

163. (new) The method of claim 162, wherein step (b) further comprises heating the at
least one site.

164. (new) The method of claim 162, wherein step (b) further comprises directing
focused acoustic energy to the at least one site.

165. (new) The method of claim 162, wherein step (b) further comprises passing an
electrical current through the at least one site.

145. (currently amended) A method for preparing a contiguous sample surface for analysis, comprising:

- (a) providing a reservoir holding an analysis-enhancing fluid;
- (b) providing a sample having a contiguous surface such that a designated site thereon is placed in droplet-receiving relationship to the fluid holding reservoir; and
- (c) applying focused acoustic energy in a manner effective to eject a droplet of the analysis-enhancing fluid from the reservoir such that the droplet is deposited on the sample surface at the designated site; and
- (d) subjecting the sample to conditions sufficient to allow the analysis-enhancing fluid to interact with the sample surface at the designated site to render the sample surface at the designated site suitable for analysis.

146. (original) The method of claim 145, wherein the analysis-enhancing fluid comprises an analysis-enhancing moiety and a carrier fluid.

147. (original) The method of claim 145, wherein the carrier fluid is evaporated from the sample surface in step (d).

148. (original) The method of claim 145, wherein the analysis-enhancing fluid is solidified on the sample surface in step (d).

149. (original) The method of claim 145, wherein the analysis-enhancing fluid comprises a mass-spectrometry matrix material.

150. (original) The method of claim 149, wherein the mass-spectrometry matrix material is a photoabsorbing matrix material.

151. (original) The method of claim 145, wherein step (c) is repeated such that a plurality of droplets is deposited on the sample surface.

152. (currently amended) The method of claim ~~141~~151, wherein the plurality of droplets is deposited on the sample surface at the same designated site.

153. (currently amended) The method of claim ~~141~~151, wherein the plurality of droplets is deposited on the sample surface at different designated sites.

154. (currently amended) The method of claim ~~143~~153, wherein the different designated sites form an array.

155. (original) The method of claim 151, wherein step (a) comprises providing a plurality of reservoirs each holding a different analysis-enhancing fluid and step (c) comprises applying focused acoustic energy in a manner effective to eject a droplet of fluid from each reservoir such that the droplets are deposited on the sample surface.

156. (currently amended) The method of claim 145, further comprising, after step (d), (e) applying sufficient energy to the designated site to ionize and release ~~the a sample molecules~~molecule from the designated site of the sample surface for analysis.

157. (currently amended) The method of claim ~~156~~166, wherein step (e) comprises bombarding the designated site with photons.

158. (original) The method of claim 157, wherein photonic bombardment is carried out using a laser.

159. (original) The method of claim 156, further comprising, after step (e), (f) determining the molecular weight of the ionized sample molecules.

166. (new) The method of claim 156, wherein step (e) comprises bombarding the designated site with photons, electrons, ions, or combinations thereof.

167. (new) The method of claim 166, wherein step (e) further comprises heating the designated site.

168. (new) The method of claim 166, wherein step (e) further comprises directing focused acoustic energy to the designated site.

169. (new) The method of claim 166, wherein step (e) further comprises passing an electrical current through the designated site.